

REMARKS

Claims 20 and 21 have been cancelled without prejudice. Claims 11 and 19 have been amended. Support for the amendments to claims 11 and 19 can be found, for example, on pages 22-23, Example 8, and on page 10, lines 13-16 of the specification as filed.

35 U.S.C. § 112, ¶ 1 -

The Examiner has rejected claims 20 and 21 under 35 U.S.C. § 112, ¶ 1, as failing to comply with the written description requirement. The Examiner contends that the phrase “wherein the DNA content of the liver basement membrane is 0.429 micrograms of DNA or less per milligram of dry weight,” is considered new matter. The Examiner argues that the data on page 22, Example 8, of the specification as filed, shows DNA amounts in the range of 0.049 to 0.809 (i.e., an average of 0.429 and standard deviation of 0.380) for purified LBM with PPA treatment. Applicants have cancelled claims 20 and 21. Accordingly, the Examiner’s rejection under 35 U.S.C. § 112, ¶ 1, has been rendered moot. Withdrawal of the rejection of claims 20 and 21 under 35 U.S.C. § 112, ¶ 1, is respectfully requested.

35 U.S.C. § 103(a) -

(1) The Examiner has rejected claims 19 and 21 under 35 U.S.C. § 103 as being obvious over Robinson et al. (*European Journal of Biochemistry/FEBS*, 11(2): 485-490) in view of U.S. Patent No. 6,866,686 (“Ollerenshaw et al.”) or U.S. Patent No. 6,734,018 (“Wolfenbarger et al.”). The Examiner contends that Robinson et al. teaches a method of isolating basement membrane from rabbit kidney using detergent. The Examiner further contends that Ollerenshaw et al. teaches a tissue graft from ureter tissue that has been

disinfected, decellularized, and treated with a nuclease to degrade associated nucleic acid, and that Wolfinbarger et al. teaches a process for producing acellular soft tissue grafts.

(2) The Examiner has rejected claims 19 and 21 under 35 U.S.C. § 103 as being obvious over Brendel et al. (*Advances in Experimental Medicine and Biology*, 131: 89-103) in view of U.S. Patent No. 6,866,686 (“Ollerenshaw et al.”) or U.S. Patent No. 6,734,018 (“Wolfinbarger et al.”). The Examiner contends that Brendel et al. teaches a method of isolating vascular basement membrane from several organ sources, wherein the basement membrane is decellularized. The Examiner further contends that Ollerenshaw et al. teaches a tissue graft from ureter tissue that has been disinfected, decellularized, and treated with a nuclease to degrade associated nucleic acid, and that Wolfinbarger et al. teaches a process for producing acellular soft tissue grafts.

(3) The Examiner has rejected claims 11-15 and 17-21 under 35 U.S.C. § 103 as being obvious over WO 98/25637 or U.S. Patent No. 6,379,710 (“Badylak”) in view of U.S. Patent No. 6,866,686 (“Ollerenshaw et al.”) or U.S. Patent No. 6,734,018 (“Wolfinbarger et al.”). The arguments that refer to “Badylak” in this response apply to either WO 98/25637 or U.S. Patent No. 6,379,710 because the ‘710 patent corresponds to WO 98/25637. The Examiner contends that Badylak teaches a tissue graft composition comprising liver basement membrane prepared by removing the cellular components from liver tissue. The Examiner further contends that Ollerenshaw et al. teaches a tissue graft from ureter tissue that has been disinfected, decellularized, and treated with a nuclease to degrade associated nucleic acid, and that Wolfinbarger et al. teaches a process for producing acellular soft tissue grafts.

The Examiner argues that a skilled artisan would have been motivated to combine the teachings of the cited prior art references to prepare a tissue graft structure comprising decellularized basement membrane substantially devoid of DNA (claims 11-15 and

17-19) or having a DNA content of 0.429 micrograms of DNA or less per milligram of dry weight of the basement membrane (claims 20 and 21).

Applicants have amended independent claims 11 and 19 to specify that the DNA content of the basement membrane is within a set of values with an average of 0.303 and a standard deviation of 0.263 micrograms of DNA per milligram of dry weight of the basement membrane. As suggested by the Examiner on pages 2-3 of the March 24, 2009 Office Action, support for this claim amendment can be found on page 22, Example 8, of the specification as filed. In addition, Applicants have cancelled claims 20 and 21 without prejudice.

1. THERE IS NO MOTIVATION TO COMBINE THE REFERENCES AND NO REASONABLE EXPECTATION OF SUCCESS

A. Rejections of Claims 19 and 21 over Robinson in view of Wolfinbarger et al. or Brendel in view of Wolfinbarger et al.

REFERENCES MUST BE CONSIDERED AS A WHOLE, INCLUDING PORTIONS THAT WOULD LEAD AWAY FROM THE CLAIMED INVENTION

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *See* MPEP § 2141.02 (VI); *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Regarding the rejection of claims 19 and 21 over Robinson in view of Wolfinbarger et al. and the rejection of claims 19 and 21 over Brendel et al. in view of Wolfinbarger et al., Wolfinbarger et al. teaches away from the claimed invention. Wolfinbarger et al. teaches vascular and tendinous grafts which are deliberately prepared so remodeling (*i.e.*, repopulation of the graft with host cells) is restricted resulting in slow, long-term remodeling of the graft by recipient cells post implantation (*See* column 5, line 65 through column 6, line 22 and column 7, lines 36-58 of Wolfinbarger et al.). The grafts are treated with a strongly anionic detergent, such as sodium dodecylsulfate, to leave a strongly anionic charge

that restricts recellularization of the graft post implantation (*See* Wolfinbarger et al., column 7, lines 32-49).

Applicants' amended claims require that the "graft composition is remodelable upon implantation" in complete contrast to Wolfinbarger et al. which teaches that remodeling should be deliberately restricted upon implantation. Thus, Wolfinbarger et al. teaches away from the claimed invention and is an unavailing reference. Accordingly, claims 19 and 21 are not obvious over the combinations of Robinson and Wolfinbarger et al., and Brendel and Wolfinbarger et al., because Wolfinbarger et al. teaches away from the claimed invention.

B. Rejection of claims 11-15 and 17-21 over Badylak in view of Wolfinbarger et al.

**REFERENCES CANNOT BE COMBINED WHERE REFERENCE TEACHES
AWAY FROM THEIR COMBINATION**

It is improper to combine references where the references teach away from their combination. *See* MPEP § 2145; *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). Regarding the rejection of claims 11-15 and 17-21 over Badylak in view of Wolfinbarger et al., Wolfinbarger et al. not only teaches away from the claimed invention, but Wolfinbarger et al. also teaches away from combination with Badylak. Wolfinbarger et al. teaches vascular and tendinous grafts which are deliberately prepared so remodeling (*i.e.*, repopulation of the graft with host cells) is restricted resulting in slow, long-term remodeling of the graft by recipient cells post implantation (see column 5, line 65 through column 6, line 22 and column 7, lines 36-58). The grafts are treated with a strongly anionic detergent, such as sodium dodecylsulfate, to leave a strongly anionic charge that restricts recellularization of the graft post implantation (*See* Wolfinbarger et al., column 7, lines 32-49).

In contrast, Badylak teaches tissue graft compositions comprising liver basement membrane for use to rapidly promote endogenous tissue growth *in vivo* upon implantation. For example, it is stated in Badylak that "[t]he tissue graft compositions formed

and used in accordance with this invention, upon implantation, undergo biological remodeling” and “serve as a rapidly vascularized matrix for supporting the growth of new endogenous connective tissue” (See column 5, lines 1-5 of Badylak). It is also stated in Badylak that “[i]t is anticipated that liver basement membrane is capable of inducing host tissue proliferation, remodeling and regeneration of appropriate tissue structures upon implantation in a number of microenvironments in vivo (e.g., tendon, ligament; bone, articular cartilage, artery, and vein)” (See column 8, line 65 through column 9, line 2 of Badylak). Therefore, Wolfinbarger et al. teaches away from combination with Badylak, because the grafts in Wolfinbarger et al. are treated with a strongly anionic detergent to restrict recellularization of the graft post implantation. In contrast, the graft constructs of Badylak are rapidly remodeled. Thus, Badylak and Wolfinbarger et al. cannot be combined because Wolfinbarger et al. teaches away from combination with Badylak. Accordingly, claims 11-15 and 17-21 are not obvious over Badylak in combination with Wolfinbarger et al.

C. Rejection of claims 11-15 and 17-21 over Badylak in view of Wolfinbarger et al.

**PROPOSED MODIFICATION CANNOT RENDER PRIOR ART
UNSATISFACTORY FOR ITS INTENDED PURPOSE**

Additionally, if the Examiner’s proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. See MPEP §2143.01; *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). If the graft composition described in Badylak was combined with the strongly anionic detergent required by the method of Wolfinbarger et al., the method described in Wolfinbarger et al. would render Badylak unsatisfactory for its intended purpose as a graft composition for promoting rapid remodeling of tissues upon implantation. Thus, as discussed above, Badylak and Wolfinbarger et al. cannot be combined,

and claims 11-15 and 17-21 are not obvious over Badylak in combination with Wolfinbarger et al.

D. Rejection of claims 11-15 and 17-21 over Badylak in view of Ollerenshaw et al.

The combination of Badylak and Ollerenshaw et al. does not overcome the insufficiencies of Badylak and Wolfinbarger et al. because Ollerenshaw et al. does not even mention basement membranes. Ollerenshaw et al. describes a purification method for application to whole animal tissue. Ollerenshaw et al. does not suggest that the method described in Ollerenshaw et al. could be applied to isolated basement membranes to achieve a purified basement membrane composition as claimed. Moreover, the method described in Ollerenshaw et al. merely describes a method of using nucleases to degrade nuclear material. Ollerenshaw et al. does not mention any specific amount of DNA that is removed by the nuclease treatment. Therefore, Ollerenshaw et al. provides no suggestion that the described method could be applied to isolated basement membranes to achieve a purified basement membrane composition with a DNA content within a set of values with an average of 0.303 and a standard deviation of 0.263 micrograms of DNA per milligram of dry weight of the basement membrane as claimed. Thus, Applicants' claims 11-15 and 17-19 are not obvious over Badylak in combination with Ollerenshaw et al.

2. ALL THE CLAIM LIMITATIONS MUST BE TAUGHT OR SUGGESTED BY THE PRIOR ART

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Therefore, in order for Applicants' invention to be rendered obvious under 35 U.S.C. § 103, the combination of references relied upon by the Examiner must teach each and every element of Applicants' invention, as defined by the claims. In this regard, all of the claimed elements were not known in the prior art.

A. Rejection of claims 19 and 21 over Robinson in view of Ollerenshaw et al. and Brendel et al. in view of Ollerenshaw et al.

The combinations of Robinson and Ollerenshaw et al. or Brendel et al. and Ollerenshaw et al. fail because these reference combinations do not teach a “basement membrane graft composition” as claimed. Neither Robinson nor Brendel et al. teaches basement membranes *for use as a graft composition*. Robinson and Brendel et al. both teach methods of isolating basement membranes, but only for the purpose of structural analysis of the isolated basement membranes. Ollerenshaw et al. does not teach basement membranes for use as a graft composition. Ollerenshaw et al. does not even mention basement membranes. Thus, the reference combinations of Robinson and Ollerenshaw et al., and Brendel et al. and Ollerenshaw et al. do not teach or suggest the use of basement membranes *as a graft composition*. Accordingly, these reference combinations do not teach all of the claim limitations (i.e., a “basement membrane graft composition”) and claims 19 and 21 cannot be obvious over the two cited prior art combinations.

B. Rejections of Claims 11-15 and 17-19

All of the claim limitations are not taught by the prior art because the prior art does not teach the DNA content required by the amended claims. Amended claims 11-15 and 17-19 specify that the DNA content of the basement membrane is within a set of values with an average of 0.303 and a standard deviation of 0.263 micrograms of DNA per milligram of dry weight of the basement membrane. None of the cited prior art references suggest a DNA content that is within a set of values with an average of 0.303 and a standard deviation of 0.263 micrograms of DNA per milligram of dry weight of the basement membrane. A DNA content that is within a set of values with an average of 0.303 and a standard deviation of 0.263 was not predictable or identified in the prior art, and there is no suggestion in the prior art that would lead a skilled artisan to choose the specific DNA content as claimed. Therefore, based

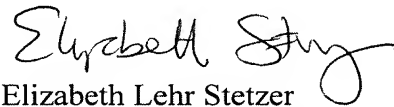
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on all of the foregoing arguments, amended claims 11-15 and 17-19 of the instant application are not obvious over the cited prior art combinations. Withdrawal of the rejections of claims 11-15 and 17-19 under 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

The foregoing amendments and remarks are believed to fully respond to the Examiner's rejections. The claims are in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance.

Respectfully submitted,



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